Case Report

Corynebacterium pseudodiphtheriticum septic arthritis secondary to intra-articular injection – a case report and literature review

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This is believed to be the first report of a case of septic arthritis, secondary to intra-articular injection, caused by Corynebacterium pseudodiphtheriticum – a skin commensal micro-organism. Review of the literature highlights the rarity of this pathogen in osteoarticular infections and a potential for delayed diagnosis and inadequate treatment due to subtle initial presentation.

Introduction

Corynebacteria are Gram-positive, aerobic or facultatively anaerobic bacilli, found as normal commensals on human skin and mucosal surfaces. Although species of Corynebacterium are well recognized as a cause of bone and joint infections (Roux et al., 2004), reports of infection with Corynebacterium pseudodiphtheriticum are rare. C. pseudodiphtheriticum is generally a harmless human commensal of the upper respiratory tract and skin. It is a known opportunistic pathogen in patients with predisposing medical conditions, such as end-stage kidney disease, renal transplant, HIV infection, malignancy and hepatic cirrhosis, and most commonly causes infections of the urinary tract and respiratory tract as well as catheter-associated infections. Albeit rare, it has also been reported as the causative organism in cases of keratitis, conjunctivitis, discitis and native and prosthetic valve endocarditis (Camello et al., 2009). To our knowledge, this is the first case of C. pseudodiphtheriticum septic arthritis of a native knee joint following an intra-articular injection in a previously well patient.

Case report

A 54-year-old white male with a longstanding history of osteoarthritic arthralgia of the left knee presented to the emergency department with an acutely painful swollen left knee. He had no underlying medical condition or immunosuppression. Two weeks prior to this acute presentation, he had received an intra-articular steroid injection in his left knee, administered by a senior rheumatologist in the outpatient hospital setting. Sixteen years ago, he underwent an arthroscopic meniscectomy in the same knee, following a rugby injury.

On admission, the patient was afebrile, his pulse-rate was 80 beats min⁻¹ and his blood pressure was 110/77 mmHg. The patient displayed a C-reactive protein (CRP) level of 139 mg l⁻¹ (normal <5 mg l⁻¹), a white blood cell count (WCC) of 11.41 x 10⁹ mm⁻³ (normal 4–11 x 10⁹ mm⁻³) and an erythrocyte sedimentation rate (ESR) of 13 mm h⁻¹ (normal 0–20 mm h⁻¹). On examination, the left knee was hot with generalized joint-line tenderness, mild effusion and a limited range-of-movement (5–30°). The bulge test was positive but the tap test was negative. On arthrocentesis, 50 ml of straw-coloured fluid was aspirated and sent for microscopic analysis and microbiological culture. The Gram-stain film of the fluid showed numerous white blood cells, of which 90 % were polymorphs, but no organisms were visible. No crystals were seen under polarized light microscopy. Empirical treatment for septic arthritis was commenced, consisting of 2 g intravenous (IV) flucloxacillin every 6 hours, and the patient underwent an arthroscopic washout and synovectomy. Samples were sent for microbiological assessment.

On day two, pain in the left knee worsened, the WCC remained normal but the CRP level rose to 187.5 mg l⁻¹. On clinical examination, the left knee remained unchanged from the initial presentation. Serological screens for hepatitis B and C and HIV were negative. Autoimmune screening for rheumatoid factor and antinuclear antibodies was negative.

Over the next 3 days the pain in the patient’s knee improved and the CRP decreased to 129.2 mg l⁻¹. After 48 h of aerobic incubation, a pure culture of a Gram-positive bacillus was obtained growing heavily on the blood culture plate inoculated with the knee aspirate. Gram-positive bacilli were
also isolated from both the synovial fluid and synovial biopsy specimens collected during arthroscopic washout. The Gram-positive bacillus from each of these specimens was identified as *C. pseudodiphtheriticum* by using the API Corne system (bioMeireux; profile 3101004). Antibiotic susceptibility of the isolate was tested by using the BSAC disc susceptibility method (www.bsac.org.uk). The isolate was sensitive to methicillin, penicillin, oxacillin, vancomycin, erythromycin and gentamicin. E-tests also confirmed susceptibility to ciprofloxacin (MIC 0.25 mg l\(^{-1}\)), vancomycin (MIC 0.25 mg l\(^{-1}\)) and penicillin (MIC <0.016 mg l\(^{-1}\)). The identification and antimicrobial susceptibility were further confirmed at the Laboratory of HealthCare Associated Infections, Health Protection Agency, Colindale, London, UK, where the isolate proved to be susceptible to cefotaxime (MIC 0.064 mg l\(^{-1}\)), meropenem (MIC, 0.008 mg l\(^{-1}\)), clindamycin (MIC 0.064 mg l\(^{-1}\)), linezolid (MIC 0.25 mg l\(^{-1}\)), tetracycline (MIC 1 mg l\(^{-1}\)) and rifampicin (MIC <0.002 mg l\(^{-1}\)). In view of the clinical response to flucloxacinil, however, the antibiotic treatment with IV flucloxacinil was continued for 8 days.

On day 8, the patient complained of recurrent pain and swelling and had a temperature of 38 °C along with an elevated CRP level of 221.4 mg l\(^{-1}\). The patient underwent a further arthroscopic debridement of the knee joint and IV vancomycin (1 g 12-hourly) was administered as a substitute for IV flucloxacinil.

The clinical condition of the patient progressively improved over the next few days and on day 16 he was discharged from the hospital with 6-weeks-worth of oral flucloxacinil. Two weeks post-discharge, the range of movement in his left knee was 10–100° and his CRP level was 10. One month post-discharge, the patient’s CRP level had returned to normal with full range of movement at the knee joint.

### Discussion

Bone and joint infections caused by *C. pseudodiphtheriticum* are exceedingly rare with only two reported cases of osteitis (Roux *et al.*, 2004) and one case of septic arthritis (Kemp *et al.*, 2005). The only other published case referring to *C. pseudodiphtheriticum* is related to a prosthetic hip joint infection and the clinical significance of its isolation from superficial scrapings was questioned by its authors (von Graevenitz *et al.*, 1998).

Little information is available regarding the clinical course and treatment for the two cases of osteitis. The patient in the aforementioned case of septic arthritis (Kemp *et al.*, 2005) was on long-term steroid therapy for muscular rheumatism. He presented with purulent discharge from the portal-site following an arthroscopic washout 2 weeks prior, which was performed for knee arthralgia. He underwent arthroscopic synovectomy with excision of the fistula, received parenteral antibiotics for 2 weeks (3 days of dicloxacillin 1 g every 6 h, then 11 days of cefuroxime 1.5 g every 6 h) followed by 3 months of oral penicillin, and was hospitalized for 1 month. The patient in the present case underwent two arthroscopic debridements and received 16 days of parenteral antibiotics over an 18 day admission period. Steroid use and iatrogenic penetration of the joint are common factors between the two cases and are the most likely to be predisposing factors for joint sepsis.

Septic arthritis following intra-articular corticosteroid injection is rare. Although no clear data exist, some groups report practitioner feedback demonstrating a range of incidence from 1 : 3 000–1 : 50 000. The relatively lower rates compare favourably with the slightly higher risk of incidental bacterial arthritis at 5.7 per 100 000 inhabitants (Pal & Morris, 1999; Charalambous *et al.*, 2003). Strict aseptic technique is essential to prevent this rare but dreaded complication. Early identification and appropriate management of infectious complications help to limit functional sequelae.

The pathogenesis of septic arthritis involves interaction between bacterial characteristics and host defences (Smith & Piercy, 1995). Septic arthritis results in the destruction of cartilage due to degradation by enzymes and toxins released by the causative organism. Management of septic arthritis involves systemic antibiotic therapy and early decompression of the joint (Perry, 1999). *Staphylococcus aureus* is the most common bacterial pathogen associated with septic arthritis on native joints. Septic arthritis caused by corynebacteria is rare; although, like *Corynebacterium diphtheriae* and *Corynebacterium ulcerans*, *C. pseudodiphtheriticum* has been documented as being responsible for cutaneous infection (Cantarelli *et al.*, 2008). Therefore, as a potential skin pathogen, one should consider its potential for infecting a joint via iatrogenic inoculation. A high index of suspicion is important since Gram staining is relatively insensitive for detection of septic arthritis, with false-negative rates ranging from 25 to 50% for non-gonococcal septic arthritis (Lossos *et al.*, 1998), with an increasing sensitivity of up to 90% in synovial fluid culture.

*C. pseudodiphtheriticum* is generally susceptible to β-lactam antibiotics, such as aminoglycosides, rifampicin and vancomycin. However, susceptibility to ciprofloxacin, clindamycin and tetracycline is reported to be variable. Methicillin resistance due to alteration of the penicillin-binding proteins is common in *C. pseudodiphtheriticum* (Camello *et al.*, 2009). In the present case, *C. pseudodiphtheriticum* was susceptible to penicillin, oxacillin, vancomycin, gentamicin, erythromycin and clindamycin. Although empirical treatment with vancomycin and an aminoglycoside or fluoroquinolone might be more appropriate in healthcare-associated infectious arthritis (HAI) before culture results are known, the present case was treated with flucloxacinil in accordance with local antibiotic treatment guidelines for the empirical treatment of native joint septic arthritis. Treatment with IV flucloxacinil was continued because of the good initial clinical response it gave. A subsequent recurrence of the symptoms called for a further debridement and substitution of therapy to IV vancomycin. However, the
<table>
<thead>
<tr>
<th>Reference</th>
<th>Patient age (years) and sex</th>
<th>Joint</th>
<th>Predisposing factor or condition</th>
<th>Joint fluid</th>
<th>Blood culture</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valenstein et al. (1988)</td>
<td>49/M Knee</td>
<td>Orthopaedic surgery</td>
<td>NA</td>
<td>C. haemolyticum</td>
<td>NA</td>
<td>Penicillin, streptomycin</td>
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<td>Morrey et al. (1977)</td>
<td>65/F Hip</td>
<td>Hip surgery</td>
<td>NA</td>
<td>Propionibacterium acnes</td>
<td>NA</td>
<td>Methicillin, penicillin</td>
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<td>Norenberg et al. (1978)</td>
<td>70/M Knee</td>
<td>Monoclonal gammopathy</td>
<td>NA</td>
<td>C. pyogenes</td>
<td>NA</td>
<td>Penicillin</td>
</tr>
<tr>
<td>Guran et al. (1979)</td>
<td>2/M Hip</td>
<td>Acute leukaemia</td>
<td>NA</td>
<td>C. diphtheriae</td>
<td>NA</td>
<td>Kanamycin</td>
</tr>
<tr>
<td>Appelbaum &amp; Dossett (1982)</td>
<td>2/M Knee</td>
<td>Vascular surgery</td>
<td>175 000</td>
<td>C. xerosis</td>
<td>–</td>
<td>Ampicillin</td>
</tr>
<tr>
<td>Valenstein et al. (1988)</td>
<td>62/M Knee</td>
<td>Vascular surgery</td>
<td>60 000</td>
<td>C. kutscheri</td>
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<td>Vancomycin, cephalothin</td>
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<td>Messina et al. (1989)</td>
<td>68/F Knee</td>
<td>Polymyalgia rheumatica, intra-articular corticosteroid injections</td>
<td>NA</td>
<td>C. xerosis</td>
<td>–</td>
<td>Penicillin, cefotaxime, erythromycin</td>
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<tr>
<td>Booth et al. (1991)</td>
<td>74/M Knee</td>
<td>Vascular surgery</td>
<td>NA</td>
<td>C. xerosis</td>
<td>NA</td>
<td>Amoxicillin, rifampicin</td>
</tr>
<tr>
<td>Kerleau et al. (1992)</td>
<td>38/F Vertebra</td>
<td>Lumbar spine surgery</td>
<td>NA</td>
<td>C. xerosis</td>
<td>NA</td>
<td>Ofloxacin</td>
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<td>Damade et al. (1993)</td>
<td>49/F Wrist</td>
<td>Alcoholic cirrhosis</td>
<td>NA</td>
<td>C. diphtheriae</td>
<td>+</td>
<td>Ofloxacin</td>
</tr>
<tr>
<td>Lehnert et al. (1995)</td>
<td>NA NA</td>
<td>Endocarditis (prosthetic heart valve)</td>
<td>NA</td>
<td>C. diphtheriae</td>
<td>NA</td>
<td>NA</td>
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<tr>
<td>Present case, 2011</td>
<td>54/M Knee</td>
<td>Intra-articular corticosteroid injection</td>
<td>NA</td>
<td>C. pseudodiphtheriticum</td>
<td>+</td>
<td>Flucloxacillin, vancomycin</td>
</tr>
</tbody>
</table>

*Number of white blood cells per mm$^3$. 

Table 1. Features of cases of septic arthritis due to corynebacteria

NA, Not available.
In the present case, *C. pseudodiphtheriticum* was most probably introduced into the joint during intra-articular injection and was fully identified and characterized as the primary pathogen, having been isolated in pure culture from aseptically collected arthroscopic debridement tissue biopsies and synovial fluid aspirate. The risk of contamination resulting in opportunistic septic arthritis during intra-articular injection reiterates the importance of meticulous aseptic technique. In essence, *C. pseudodiphtheriticum* is an otherwise generally harmless normal skin commensal, but when it is introduced into a joint, it has the potential to cause septic arthritis. The benign initial presentation of articular infections in published cases and the present case is in strong contrast to the acute presentation of *S. aureus* septic arthritis and can potentially lead to a delay in diagnosis and a substandard therapeutic course of action.

At present, experience is limited to very few published cases (see Table 1), and therefore, one cannot establish this feature of clinical subtlety as being purely related to the organism, the steroid, or other variables.

In conclusion, we report a case of *C. pseudodiphtheriticum* septic arthritis following intra-articular steroid injection that highlights the importance of maintaining good aseptic technique when performing intra-articular injections and also keeping a high index of suspicion of septic arthritis post intra-articular injection.

**References**


